

## EXAMINER'S PROPOSED AMENDMENT

### DRAFT

An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicants, an amendment may be filed as provided by 37 C.F.R. §1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this Examiner's amendment was given in a telephone interview on  
xxxxxxxxxxxxxxxxxxxxxxxxxxxx with Mr. xxxxxxxxxxxxxxxxxxxx, Applicants' Representative.

#### **In the Claims:**

1. (Previously Presented) A method of producing a plurality of fused aggregates forming a desired three-dimensional structure, the method comprising: depositing a layer of a matrix on a substrate; embedding a plurality of cell aggregates, each comprising a plurality of cells, in the layer of the matrix to form a three-dimensional layered structure of claim 52, the aggregates being arranged in a non-random predetermined pattern, wherein the cell aggregates have predetermined positions in the pattern; allowing at least one aggregate of said plurality of cell aggregates to fuse with at least one other aggregate of the plurality of cell aggregates to form the desired structure; and separating the structure from the matrix.
2. (Currently Amended) The method of claim 1, wherein the layer of the matrix constitutes a first layer, the plurality of cell aggregates constitutes a first plurality of cell aggregates, and the predetermined pattern constitutes a first predetermined pattern, the method further comprising the steps of: depositing a second layer of the matrix on the first layer; and embedding a second plurality of cell aggregates in the second layer, the second plurality of cell aggregates comprising a plurality of cells, the second plurality of cell aggregates being arranged in a second predetermined pattern, and allowing at least one cell aggregate in the first plurality of cell aggregates to fuse with at least one cell aggregate in the second plurality of cell aggregates.
3. (Currently Amended) The method of claim 2, wherein the first and second predetermined patterns are substantially the same, and wherein the second plurality of cell aggregates is embedded in the second layer of the matrix in registration with the first plurality

of cell aggregates.

4. (Currently Amended) The method of claim 2, wherein the desired structure is a tube, the first and second predetermined patterns are both circular in shape, and the second plurality of cell aggregates is embedded in the second layer of the matrix in registration with the first plurality of cell aggregates.

5. (Currently Amended) The method of claim 1, wherein the thickness of the layer of the matrix is about equal to the average diameter of the plurality of cell aggregates.

6. (Currently Amended) The method of claim 1, wherein the cell aggregates are substantially spherical.

7. (Currently Amended) The method of claim 1, wherein the cell aggregates are substantially uniform in size.

8. (Currently Amended) The method of claim 1, wherein the cell aggregates have an average size between about 100 and about 600 microns.

9. (Currently Amended) The method of claim 8, wherein no more than about 10% ~~percent~~ of the cell aggregates deviate from said average size by more than 5%.

10. (Canceled)

11. (Currently Amended) The method of claim 1, wherein the cell aggregates consist essentially of cells of a single type.

12. (Currently Amended) The method of claim 1, wherein at least one of the cell aggregates comprises a plurality of living cells of a first type and a plurality of living cells of a second type that is different from the first type.

13. (Currently Amended) The method of claim 12, wherein said at least one cell aggregate comprises a mixture of said cells of the first type and said cells of the second type and the method further comprises the step of allowing at least some of the cells of the first type to segregate from at least some of the cells of the second type.

14. (Currently Amended) The method of claim 12, wherein the cells of the first type are epithelial cells and the cells of the second type are connective tissue-forming cells.
15. (Currently Amended) The method of claim 1, wherein the predetermined pattern comprises a ring.
16. (Currently Amended) The method of claim 1, wherein the matrix comprises a gel.
17. (Currently Amended) The method of claim 1, wherein said plurality of cell aggregates includes at least one cell aggregate consisting essentially of cells of a first type and at least one other cell aggregate consisting essentially of cells of a second type different from the first type.

Claims 18.–51. (Canceled)

52. (Previously presented) A three-dimensional layered structure comprising: at least one layer of a matrix; and a plurality of cell aggregates, each cell aggregate comprising a plurality of living cells; wherein the cell aggregates are embedded in the at least one layer of matrix in a non-random predetermined pattern, the cell aggregates having predetermined positions in the pattern.
53. (Previously presented) The structure of claim 52, wherein the cell aggregates are substantially uniform in size and shape.
54. (Previously presented) The structure of claim 52, wherein the cell aggregates are cylindrical.
55. (Previously presented) The structure of claim 54, wherein the cylindrical cell aggregates are from about 100 microns to about 600 microns in cross-sectional diameter.
56. (Previously presented) The structure of claim 52, wherein the cell aggregates are substantially spherical.
57. (Previously presented) The structure of claim 56, wherein the substantially spherical cell aggregates are between about 100 and about 600 microns in diameter.

58. (Previously presented) The structure of claim 52, wherein each cell aggregate comprises a plurality of living cells of a single cell type.
59. (Previously presented) The structure of claim 52, wherein at least one of the cell aggregates comprises a plurality of living cells of a first type and a plurality of living cells of a second type, the second type being different from the first type.
60. (Previously presented) The structure of claim 52, wherein the plurality of cell aggregates includes at least one cell aggregate consisting essentially of cells of a first type and at least one other cell aggregate consisting essentially of cells of a second type, the second type being different from the first type.
61. (Previously presented) The structure of claim 52, wherein the at least one layer of matrix is biocompatible and about 100 microns to about 600 microns thick.
62. (Previously presented) The structure of claim 52, wherein the at least one layer of matrix is biocompatible and selected from the group consisting of thermo-reversible gels, photo-sensitive gels, pH-sensitive gels, cell type specific gels, and combinations thereof.
63. (Previously presented) The structure of claim 52, wherein the at least one layer of matrix is biocompatible and comprises at least two different types of biocompatible matrices.
64. (Currently Amended) The structure of claim 52, comprising: a first layer of matrix; and a second layer of matrix deposited on the first layer; wherein the first layer and second layer of matrix are biocompatible; wherein the cell aggregates are embedded in the first layer and in the second layer in a predetermined pattern.
65. (Currently Amended) The structure of claim 64, further comprising at least one additional layer of matrix deposited on the second layer, wherein the at least one additional layer of matrix is biocompatible, wherein the cell aggregates are embedded in the first layer, the second layer, and the at least one additional layer in a predetermined pattern.
66. (Previously presented) The structure of claim 64, wherein the first layer comprises a type of biocompatible matrix that is different from the type of biocompatible matrix in the second layer.

Claims 67–84. (Canceled)

85. (Previously presented) The structure of claim 59, wherein the cells of the first type are smooth muscle cells and the cells of the second type are endothelial cells.

86. (Previously presented) The structure of claim 60, wherein the cells of the first type are smooth muscle cells and the cells of the second type are endothelial cells.

87. (Previously presented) The method of claim 12, wherein the cells of the first type are smooth muscle cells and the cells of the second type are endothelial cells.

88. (Previously presented) The method of claim 17, wherein the cells of the first type are smooth muscle cells and the cells of the second type are endothelial cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:00 A.M. to 5:30 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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